

Scientific Abstract

Metastatic colorectal adenocarcinoma is a rapidly fatal disease in the vast majority of affected patients despite combined modality therapy with radiation and chemotherapy. Strategies have been developed to attempt to eradicate malignant cells by stimulating a host immune response to the aberrant colon cancer cells. In this regard, a recombinant vaccinia viral vector encoding human carcinoembryonic antigen (CEA), a relevant tumor-associated antigen, is undergoing clinical trials with the goal of eliciting CEA-specific immune responses. It is the purpose of this protocol to evaluate the feasibility of eliciting CEA-specific immunity utilizing the strategy of polynucleotide vaccination. Extensive work has shown that naked plasmid DNA injected into muscles is taken up by myocytes with expression of encoded genes. Further, the expression of these genes can elicit humoral and cellular immune responses to encoded antigens. We have shown in murine models that a CEA polynucleotide vaccine can successfully elicit antibody and T cell immune responses to human CEA. Further, studies have determined threshold and optimal dosing regimens. The CEA polynucleotide vaccine has also been demonstrated to protect animals against challenge with a syngeneic murine colon carcinoma line expressing human CEA. In this present context, we will deliver a plasmid encoding the cDNA for human CEA. This plasmid will be injected intramuscularly to determine whether anti-CEA immunity can be elicited in humans by this route. It will further be determined whether this route of gene transfer to humans is safe and associated with any toxicity.